



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant(s)	Wen-Tien Chen	Examiner:	Unassigned
Serial No.:	10/727,211	Group Art Unit:	Unassigned
Filed:	December 3, 2003	Docket:	178-295 CIP/CON
For:	COMPOSITIONS AND METHODS FOR INHIBITION OF CANCER INVASION AND ANGIOGENESIS	Dated:	March 3, 2004

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

*I hereby certify this correspondence is being deposited  
with the United States Postal Service as first class mail,  
postpaid in an envelope, addressed to:  
Commissioner for Patents, P.O. Box 1450, Alexandria,  
VA 22313-1450*

20231 on March 3, 2004

Signature: \_\_\_\_\_

*Julie L. Watts*

**INFORMATION DISCLOSURE STATEMENT**

Sir:

In order to fulfill the requirements of candor and good faith set forth in 37 C.F.R. §1.56, Applicants submit herewith the following Information Disclosure Statement in accordance with the provisions of 37 C.F.R. §1.97 and §1.98.

**UNITED STATES PATENTS**

<b><u>PATENTEE</u></b>	<b><u>PATENT NO.</u></b>	<b><u>ISSUE DATE</u></b>
Bachovchin, et al.	6,258,597 B1	July 10, 2001
Carron, et al.	6,193,968 B1	February 27, 2001
Bissell, et al.	6,123,941	September 26, 2000
Hellstrom et al.	5,980,896	November 9, 1999



Hirth	5,942,385	August 24, 1999
Brooks, et al.	5,753,230	May 19, 1998
Chen	5,221,622	June 22, 1993
Yamada et al.	5,092,885	March 3, 1992
Page	5,545,405	August 13, 1996

### FOREIGN PATENT DOCUMENTS

<u>COUNTRY</u>	<u>PUBLICATION NO.</u>	<u>PUBLICATION DATE</u>
PCT	WO 96/38550	December 5, 1996

### NON-PATENT PUBLICATIONS

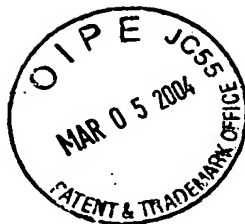
1. J. Heins, P. Welker, Chr. Schönlein, I. Born, B. Hartrodt, K. Neubert, D. Tsuru and A. Barth, "Mechanism of proline-specific proteinases: (I) substrate specificity of dipeptidyl peptidase IV from pig kidney and proline-specific endopeptidase from *Flavobacterium meningosepticum*," *Biochimica et Biophysica Acta* (1988) 954:161-169.
2. Wen-Tien Chen and Jaw-Yuan Wang, "Specialized Surface Protrusions of Invasive Cells, Invadopodia and Lamellipodia, Have Differential MT1-MMP, MMP-2, and TIMP-2 Localization," *Annals of the New York Acad. Of Sciences* (1999) 878: 361-371.
3. Susette C. Mueller, Giulio Gherzi, Steven K. Akiyama, Qing-Xiang Amy Sang, Linda Howard, Mayra Pineiro-Sanchez, Hirokazu Nakahara, Yunyun Yeh, and Wen-Tien Chen, "A Novel Protease-docking Function of Integrin at Invadopodia", *The Journal of Biological Chemistry* (1999) 274/35: 24947-24952.
4. Donald Ingber and Judah Folkman, "Inhibition of Angiogenesis Through Modulation of Collagen Metabolism," *Laboratory Investigation*. (1988) 59/1:. 44-51.
5. Marsha A. Moses, Judith Sudhalter, Robert Langer, "Identification of an Inhibitor of Neovascularization from Cartilage," *Science* 1990, 248: 1408-1410.



6. Christine H. Blood and Bruce R. Zetter, "Tumor interactions with the vasculature: angiogenesis and tumor metastasis," *Biochimica et Biophysica Acta* (1990) 1032: 89-118.
7. Leslie A. Goldstein and Wen-Tien Chen, "Identification of an Alternatively Spliced Seprase mRNA That Encodes a Novel Intracellular Isoform," *The Journal of Biological Chemistry* (2000) 275/4: 2554-2559.
8. Wanda Auerbach and Robert Auerbach, "Angiogenesis Inhibition: A Review," *Pharmac. Ther.* (1994) 63: 265-311.
9. Rakesh K. Jain, "Vascular and interstitial barriers to delivery of therapeutic agents in tumors," *Cancer and Metastasis Reviews* (1990) 9: 253-266.
10. Sally S. Seaver, Ph.D., "Monoclonal Antibodies in Industry: More Difficult Than Originally Thought," *Genetic Engineering News* (1994) 14/14: 10 and 21.
11. William J. Harris and Steven Emery, "Therapeutic antibodies – the coming of age," *Trends in Biotechnology* (1993) 11: 42-44.
12. Trisha Gura "Systems for Identifying New Drugs Are Often Faulty," *Science*(1997) 278: 1041-1042.
13. Eryl Liddell and Ian Weeks "Antibody Technology" *Bios Scientific Publishers* (1995) 23-44.
14. Sabine Hartel-Schenk, Nikolaus Loch, Martin Zimmermann and Werner Reutter, "Development of monoclonal antibodies against different protein and carbohydrate epitopes of dipeptidyl peptidase IV from rat liver plasma membranes," *Eur. J. Biochem* (1991) 196: 349-355.
15. Dirk Reinhold, Ute Bank, Frank Bühling, Klaus Neubert, Taila Mattern, Artur Jochen Ulmer, Hans-Dieter Flad, and Siegfried Ansorge, "Dipeptidyl Peptidase IV (CD26) on Human Lymphocytes. Synthetic Inhibitors of and Antibodies against Dipeptidyl Peptidase IV Suppress the Proliferation of Pokeweed Mitogen-Stimulated Peripheral Blood Mononuclear Cells, and IL-2 and IL-6 Production," *Immunobiology* (1993) 188: 403-414.
16. J.J. Van Den Oord, "Expression of CD26/dipeptidyl-peptidase IV in benign and malignant pigment-cell lesions of the skin," *British Journal of Dermatology* (1998) 138: 615-621.
17. Hung-Chi Cheng, Mossaad Abdel-Ghany, Randolph C. Elble, and Bendicht U. Pauli, "Lung Endothelial Dipeptidyl Peptidase IV Promotes Adhesion and Metastasis of Rat Breast Cancer Cells via Tumor Cell Surface-associated Fibronectin," *The Journal of Biological Chemistry* (1998) 273/37: 24207-24215.



18. T. Mattern, A. C. Feller, B. Kniep, H. -D. Flad, and A. J. Ulmer, "Comparative studies on three monoclonal antibodies (anti DPPIV, anti Ta1, IOT15) recognizing antigens clustered in CDw26," *Immunobiology* (1988) 178(1/2): 110, Abstract H.12.
19. Arao, Shuichi, et al., " $\beta$ 1 Integrins Play an Essential Role in Adhesion and Invasion of Pancreatic Carcinoma Cells", *Pancreas* 2000, 20(2):129-137.
20. Barbet, Jacques, et al., "Pretargeting with the Affinity Enhancement System for Radioimmunotherapy", *Cancer Biotherapy & Radiopharmaceuticals* 1999, 14(3):153-166.
21. Duke-Cohan, Jonathan, et al., "Targeting of an Activated T-Cell Subset Using a Bispecific Antibody-Toxin Conjugate Directed Against CD4 and CD26", *Blood* 1993, 82(7):2224-2234.
22. Elble, R.C., et al., "Lu-ECAM-1 and DPP IV in Lung Metastasis", *Curr. Top Microbiol Immunol* 1996, 213(1):107-122.
23. Fukushima, Yuji, et al., "Integrin  $\alpha$ 3 $\beta$ 1-Mediated Interaction with Laminin-5 Stimulates Adhesion, Migration and Invasion of Malignant Glioma Cells", *Int. J. Cancer* 1998, 76:63-72.
24. Abdel-Ghany, Mossaad, et al., "Truncated Dipeptidyl Peptidase IV is a Potent Anti-Adhesion and Anti-Metastasis Peptide for Rat Breast Cancer Cells", *Invasion Metastasis* 1998, 18:35-43.
25. Gherzi, Guilio, et al., "Critical role of dipeptidyl peptidase IV in neuropeptide Y-mediated endothelial cell migration in response to wounding", *Peptides* 2001, 22:453-458.
26. Johnson, Robert C., et al., "Lung Endothelial Dipeptidyl IV is an Adhesion Molecule for Lung-metastatic Rat Breast and Prostate Carcinoma Cells", *The Journal of Cell Biology* 1993, 121(6):1423-1432.
27. Klominek, Julius, et al., "Differential Motile Response of Human Malignant Mesothelioma Cells to Fibronectin, Laminin and Collagen Type IV: The Role of  $\beta$ 1 Integrins", *Int. J. Cancer* 1997, 72:1034-1044.
28. Kotani, T., et al., "Diagnostic Usefulness of Dipeptidyl Aminopeptidase IV Monoclonal Antibody in Paraffin-Embedded Thyroid Follicular Tumours", *Journal of Pathology* 1992, 168:41-45.
29. Lundstrom, Ase, et al., "The Role of  $\alpha$ 2 $\beta$ 1 and  $\alpha$ 3 $\beta$ 1 Integrin Receptors in the Initial Anchoring of MDA-MB-231 Human Breast Cancer Cells to Cortical Bone Matrix", *Biochemical and Biophysical Research Communications* 1998, 250:735-740.



30. Masumoto, Akihhide, et al., "Role of  $\beta 1$  Integrins in Adhesion and Invasion of Hepatocellular Carcinoma Cells", *Hepatology* 1999, 29(1):68-74.
31. Schroder, Soren, et al., "Carcinoembryonic Antigen and Nonspecific Cross-Reacting Antigen in Thyroid Cancer", *The American Journal of Surgical Pathology* 1987, 11(2):100-108.

The above-referenced documents are listed on PTO Form 1449. We have enclosed the cited documents to facilitate reference to them.

Applicants are not aware of any other references to be identified at this time. If the Examiner has any questions or comments relating to the present application, he or she is respectfully invited to contact Applicants' agent at the telephone number set forth below.

Respectfully submitted,

Edna I. Gergel, Ph.D.  
Registration No.: 50,819  
Agent for Applicant(s)

HOFFMANN & BARON, LLP  
6900 Jericho Turnpike  
Syosset, New York 11791  
(516) 822-3550  
EIG:jlw

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE  
(Rev. 2-32) PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
178-295 CIP/CONSERIAL NO.  
10/727,211INFORMATION DISCLOSURE  
STATEMENT BY APPLICANTAPPLICANT  
Wen-Tien ChenCONFIRMATION NO.  
Unassigned

(Use several sheets if necessary)

FILING DATE  
December 3, 2003GROUP  
Unassigned

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
		6,258,597 B1	7/10/01	Bachovchin, et al.			
		6,193,968 B1	2/27/01	Carron, et al.			
		6,123,941	9/26/00	Bissell, et al.			
		5,980,896	11/9/99	Hellstrom et al.			
		5,942,385	8/24/99	Hirth			
		5,753,230	5/19/98	Brooks, et al.			
		5,221,622	6/22/93	Chen			
		5,092,885	3/3/92	Yamada et al.			
		5,545,405	8/13/96	Page			

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO
		WO96/38550	12-1996	PCT				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		J. Heins, P. Welker, Chr. Schönlein, I. Born, B. Hartrodt, K. Neubert, D. Tsuru and A. Barth, "Mechanism of proline-specific proteinases: (I) substrate specificity of dipeptidyl peptidase IV from pig kidney and proline-specific endopeptidase from <i>Flavobacterium meningosepticum</i> ," <i>Biochimica et Biophysica Acta</i> (1988) 954:161-169.
--	--	--

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (Rev. 2-32) PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 178-295 CIP/CON	SERIAL NO. 10/727,211
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT Wen-Tien Chen	CONFIRMATION NO. Unassigned
(Use several sheets if necessary)	FILING DATE December 3, 2003	GROUP Unassigned

		Wen-Tien Chen and Jaw-Yuan Wang, "Specialized Surface Protrusions of Invasive Cells, Invadopodia and Lamellipodia, Have Differential MT1-MMP, MMP-2, and TIMP-2 Localization," <i>Annals of the New York Acad. Of Sciences</i> (1999) <u>878</u> : 361-371.
		Susette C. Mueller, Giulio Gherzi, Steven K. Akiyama, Qing-Xiang Amy Sang, Linda Howard, Mayra Pineiro-Sanchez, Hirokazu Nakahara, Yunyun Yeh, and Wen-Tien Chen, "A Novel Protease-docking Function of Integrin at Invadopodia", <i>The Journal of Biological Chemistry</i> (1999) <u>274/35</u> : 24947-24952.
		Donald Ingber and Judah Folkman, "Inhibition of Angiogenesis Through Modulation of Collagen Metabolism," <i>Laboratory Investigation.</i> (1988) <u>59/1</u> : 44-51.
		Marsha A. Moses, Judith Sudhalter, Robert Langer, "Identification of an Inhibitor of Neovascularization from Cartilage," <i>Science</i> 1990, <u>248</u> : 1408-1410.
		Christine H. Blood and Bruce R. Zetter, "Tumor interactions with the vasculature: angiogenesis and tumor metastasis," <i>Biochimica et Biophysica Acta</i> (1990) <u>1032</u> : 89-118.
		Leslie A. Goldstein and Wen-Tien Chen, "Identification of an Alternatively Spliced Seprase mRNA That Encodes a Novel Intracellular Isoform," <i>The Journal of Biological Chemistry</i> (2000) <u>275/4</u> : 2554-2559.
		Wanda Auerbach and Robert Auerbach, "Angiogenesis Inhibition: A Review," <i>Pharmac. Ther.</i> (1994) <u>63</u> : 265-311.
		Rakesh K. Jain, "Vascular and interstitial barriers to delivery of therapeutic agents in tumors," <i>Cancer and Metastasis Reviews</i> (1990) <u>9</u> : 253-266.
		Sally S. Seaver, Ph.D., "Monoclonal Antibodies in Industry: More Difficult Than Originally Thought," <i>Genetic Engineering News</i> (1994) <u>14/14</u> : 10 and 21.

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (Rev. 2-32) PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 178-295 CIP/CON	SERIAL NO. 10/727,211
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT Wen-Tien Chen	CONFIRMATION NO. Unassigned
(Use several sheets if necessary)	FILING DATE December 3, 2003	GROUP Unassigned

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		William J. Harris and Steven Emery, "Therapeutic antibodies – the coming of age," <i>Trends in Biotechnology</i> (1993) <u>11</u> : 42-44.
		Trisha Gura "Systems for Identifying New Drugs Are Often Faulty," <i>Science</i> (1997) <u>278</u> : 1041-1042.
		Eryl Liddell and Ian Weeks "Antibody Technology" <i>Bios Scientific Publishers</i> (1995) 23-44.
		Sabine Hartel-Schenk, Nikolaus Loch, Martin Zimmermann and Werner Reutter, "Development of monoclonal antibodies against different protein and carbohydrate epitopes of dipeptidyl peptidase IV from rat liver plasma membranes," <i>Eur. J. Biochem</i> (1991) <u>196</u> : 349-355.
		Dirk Reinhold, Ute Bank, Frank Bühling, Klaus Neubert, Taila Mattern, Artur Jochen Ulmer, Hans-Dieter Flad, and Siegfried Ansorge, "Dipeptidyl Peptidase IV (CD26) on Human Lymphocytes. Synthetic Inhibitors of and Antibodies against Dipeptidyl Peptidase IV Suppress the Proliferation of Pokeweed Mitogen-Stimulated Peripheral Blood Mononuclear Cells, and IL-2 and IL-6 Production," <i>Immunobiology</i> (1993) <u>188</u> : 403-414.
		J.J. Van Den Oord, "Expression of CD26/dipeptidyl-peptidase IV in benign and malignant pigment-cell lesions of the skin," <i>British Journal of Dermatology</i> (1998) <u>138</u> : 615-621.
		Hung-Chi Cheng, Mossaad Abdel-Ghany, Randolph C. Elble, and Bendicht U. Pauli, "Lung Endothelial Dipeptidyl Peptidase IV Promotes Adhesion and Metastasis of Rat Breast Cancer Cells via Tumor Cell Surface-associated Fibronectin," <i>The Journal of Biological Chemistry</i> (1998) <u>273/37</u> : 24207-24215.
		T. Mattern, A. C. Feller, B. Kniep, H. -D. Flad, and A. J. Ulmer, "Comparative studies on three monoclonal antibodies (anti DPPIV, anti Ta1, IOT15) recognizing antigens clustered in CDw26," <i>Immunobiology</i> (1988) <u>178(1/2)</u> : 110, Abstract H.12.

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.



FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (Rev. 2-32) PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 178-295 CIP/CON	SERIAL NO. 10/727,211
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT Wen-Tien Chen	CONFIRMATION NO. Unassigned
(Use several sheets if necessary)	FILING DATE December 3, 2003	GROUP Unassigned

		Arao, Shuichi, et al., " $\beta$ 1 Integrins Play an Essential Role in Adhesion and Invasion of Pancreatic Carcinoma Cells", <i>Pancreas</i> 2000, <u>20</u> (2):129-137.
		Barbet, Jacques, et al., "Pretargeting with the Affinity Enhancement System for Radioimmunotherapy", <i>Cancer Biotherapy &amp; Radiopharmaceuticals</i> 1999, <u>14</u> (3):153-166.
		Duke-Cohan, Jonathan, et al., "Targeting of an Activated T-Cell Subset Using a Bispecific Antibody-Toxin Conjugate Directed Against CD4 and CD26", <i>Blood</i> 1993, <u>82</u> (7):2224-2234.
		Elble, R.C., et al., "Lu-ECAM-1 and DPP IV in Lung Metastasis", <i>Curr. Top Microbiol Immunol</i> 1996, <u>213</u> (1):107-122.
		Fukushima, Yuji, et al., "Integrin $\alpha$ 3 $\beta$ 1-Mediated Interaction with Laminin-5 Stimulates Adhesion, Migration and Invasion of Malignant Glioma Cells", <i>Int. J. Cancer</i> 1998, <u>76</u> :63-72.
		Abdel-Ghany, Mossaad, et al., "Truncated Dipeptidyl Peptidase IV is a Potent Anti-Adhesion and Anti-Metastasis Peptide for Rat Breast Cancer Cells", <i>Invasion Metastasis</i> 1998, <u>18</u> :35-43.
		Gherzi, Guilio, et al., "Critical role of dipeptidyl peptidase IV in neuropeptide Y-mediated endothelial cell migration in response to wounding", <i>Peptides</i> 2001, <u>22</u> :453-458.
		Johnson, Robert C., et al., "Lung Endothelial Dipeptidyl IV is an Adhesion Molecule for Lung-metastatic Rat Breast and Prostate Carcinoma Cells", <i>The Journal of Cell Biology</i> 1993, <u>121</u> (6):1423-1432.
		Klominek, Julius, et al., "Differential Motile Response of Human Malignant Mesothelioma Cells to Fibronectin, Laminin and Collagen Type IV: The Role of $\beta$ 1 Integrins", <i>Int. J. Cancer</i> 1997, <u>72</u> :1034-1044.
		Kotani, T., et al., "Diagnostic Usefulness of Dipeptidyl Aminopeptidase IV Monoclonal Antibody in Paraffin-Embedded Thyroid Follicular Tumours", <i>Journal of Pathology</i> 1992, <u>168</u> :41-45.

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (Rev. 2-32) PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 178-295 CIP/CON	SERIAL NO. 10/727,211
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT Wen-Tien Chen	CONFIRMATION NO. Unassigned
(Use several sheets if necessary)	FILING DATE December 3, 2003	GROUP Unassigned

			Lundstrom, Ase, et al., "The Role of $\alpha 2 \beta 1$ and $\alpha 3 \beta 1$ Integrin Receptors in the Initial Anchoring of MDA-MB-231 Human Breast Cancer Cells to Cortical Bone Matrix", <i>Biochemical and Biophysical Research Communications</i> 1998, <u>250</u> :735-740.
			Masumoto, Akihide, et al., "Role of $\beta 1$ Integrins in Adhesion and Invasion of Hepatocellular Carcinoma Cells", <i>Hepatology</i> 1999, <u>29</u> (1):68-74.
			Schroder, Soren, et al., "Carcinoembryonic Antigen and Nonspecific Cross-Reacting Antigen in Thyroid Cancer", <i>The American Journal of Surgical Pathology</i> 1987, <u>11</u> (2):100-108.

185755\_1

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.